



ISCU gene

iron-sulfur cluster assembly enzyme

Normal Function

The *ISCU* gene provides instructions for making a protein called the iron-sulfur cluster assembly enzyme. As its name suggests, this enzyme is involved in the formation of clusters of iron and sulfur atoms (Fe-S clusters). Specifically, the enzyme acts as a platform, or scaffold, for the assembly of these clusters. Fe-S clusters are critical for the function of many different proteins, including those needed for DNA repair and the regulation of iron levels. Proteins containing Fe-S clusters are also necessary for energy production within mitochondria, which are the cell structures that convert the energy from food into a form that cells can use.

Health Conditions Related to Genetic Changes

myopathy with deficiency of iron-sulfur cluster assembly enzyme

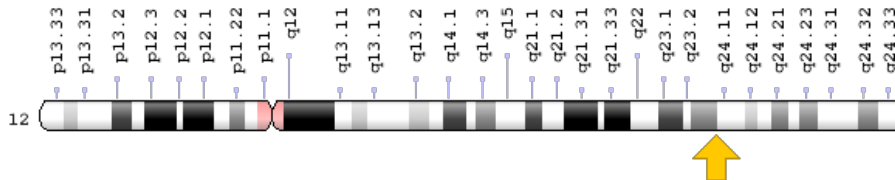
At least two mutations in the *ISCU* gene have been found to cause myopathy with deficiency of iron-sulfur cluster assembly enzyme. The more common mutation, written as IVS5+382G>C, alters the way the gene's instructions are pieced together to produce the enzyme. Most affected individuals have this mutation in both copies of the *ISCU* gene in each cell. The other mutation, which has been identified in one family, replaces the amino acid glycine with the amino acid glutamate at position 50 in the enzyme (written as Gly50Glu or G50E). Affected individuals in this family have had the G50E mutation in one copy of the *ISCU* gene in each cell and the IVS5+382G>C mutation in the other copy of the gene. This combination of mutations causes a severe variant of the disorder characterized by progressive muscle weakness and wasting.

Mutations in the *ISCU* gene severely limit the amount of iron-sulfur cluster assembly enzyme that is made in cells. A shortage of this enzyme prevents the normal production of proteins that contain Fe-S clusters, which disrupts a variety of cellular activities. A reduction in the amount of iron-sulfur cluster assembly enzyme is particularly damaging to skeletal muscle cells. Within the mitochondria of these cells, a lack of this enzyme causes problems with energy production and an overload of iron. These defects lead to muscle weakness, pain, and the other features of myopathy with deficiency of iron-sulfur cluster assembly enzyme.

Chromosomal Location

Cytogenetic Location: 12q23.3, which is the long (q) arm of chromosome 12 at position 23.3

Molecular Location: base pairs 108,561,463 to 108,569,384 on chromosome 12 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- HML
- hnifU
- iron-sulfur cluster scaffold homolog (E. coli)
- IscU
- IscU iron-sulfur cluster scaffold homolog
- ISCU_HUMAN
- ISU2
- MGC74517
- NIFU
- NifU-like N-terminal domain containing
- NIFUN
- nitrogen fixation cluster-like

Additional Information & Resources

Educational Resources

- Molecular Cell Biology (fourth edition, 2000): Three-dimensional structures of some iron-sulfur clusters in electron-transporting proteins (figure)
<https://www.ncbi.nlm.nih.gov/books/NBK21528/?rendertype=figure&id=A4387>

GeneReviews

- Myopathy with Deficiency of ISCU
<https://www.ncbi.nlm.nih.gov/books/NBK5299>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ISCU%5BTIAB%5D%29+OR+%28iron-sulfur+cluster+%5Btiab%5D+AND+scaffold+%5Btiab%5D%29%29+OR+%28iron-sulfur+cluster+%5Btiab%5D+AND+assembly+%5Btiab%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D>

OMIM

- IRON-SULFUR CLUSTER SCAFFOLD, E. COLI, HOMOLOG OF
<http://omim.org/entry/611911>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_ISCU.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=ISCU%5Bgene%5D>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=29882
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/23479>
- UniProt
<http://www.uniprot.org/uniprot/Q9H1K1>

Sources for This Summary

- Kollberg G, Tulinius M, Melberg A, Darin N, Andersen O, Holmgren D, Oldfors A, Holme E. Clinical manifestation and a new ISCU mutation in iron-sulphur cluster deficiency myopathy. *Brain*. 2009 Aug;132(Pt 8):2170-9. doi: 10.1093/brain/awp152. Epub 2009 Jun 30.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19567699>
- Li K, Tong WH, Hughes RM, Rouault TA. Roles of the mammalian cytosolic cysteine desulfurase, ISCS, and scaffold protein, ISCU, in iron-sulfur cluster assembly. *J Biol Chem*. 2006 May 5;281(18):12344-51. Epub 2006 Mar 9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16527810>

- Mochel F, Knight MA, Tong WH, Hernandez D, Ayyad K, Taivassalo T, Andersen PM, Singleton A, Rouault TA, Fischbeck KH, Haller RG. Splice mutation in the iron-sulfur cluster scaffold protein ISCU causes myopathy with exercise intolerance. *Am J Hum Genet.* 2008 Mar;82(3):652-60. doi: 10.1016/j.ajhg.2007.12.012. Epub 2008 Feb 14.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18304497>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2427212/>
- Olsson A, Lind L, Thornell LE, Holmberg M. Myopathy with lactic acidosis is linked to chromosome 12q23.3-24.11 and caused by an intron mutation in the ISCU gene resulting in a splicing defect. *Hum Mol Genet.* 2008 Jun 1;17(11):1666-72. doi: 10.1093/hmg/ddn057. Epub 2008 Feb 23.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18296749>
- Rouault TA, Tong WH. Iron-sulfur cluster biogenesis and human disease. *Trends Genet.* 2008 Aug;24(8):398-407. doi: 10.1016/j.tig.2008.05.008. Epub 2008 Jul 5. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18606475>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2574672/>
- Tong WH, Rouault TA. Functions of mitochondrial ISCU and cytosolic ISCU in mammalian iron-sulfur cluster biogenesis and iron homeostasis. *Cell Metab.* 2006 Mar;3(3):199-210.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16517407>

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